

Remarks

At page 5 of the Official Action, the Examiner has objected to claims 49-51, 57 and 58 for reciting "A method" or "A host cell". The claims have been amended as required by the Examiner thereby obviating this ground of objection.

Claim 7 has been objected to as a substantial duplicate of claim 1. Claim 7 has been canceled, thereby rendering this ground of objection moot.

Claims 45-51 and 56-58 are objected to for reciting sequences which are currently being withheld from consideration. The claims have been amended to eliminate recitation of SEQ ID NOS: 3, 5, and 7 in compliance with the Examiner's requirement.

**CLAIMS 4 AND 6 AS AMENDED MEET THE REQUIREMENTS OF 35 U.S.C.
§112, SECOND PARAGRAPH**

The Examiner has rejected claims 4 and 6 under 35 U.S.C. §112, second paragraph for alleged indefiniteness. Specifically, the Examiner asserts that claim 2, from which claim 4 depends, reads on a DNA molecule having the sequence of SEQ ID NO: 1 and thus must lack intronic sequences.

Accordingly, Applicants have amended claim 4 such that it is in independent form wherein the exons of the isolated nucleic acid are identical to SEQ ID NO: 1 and encode a MOAT-B protein. This amendment eliminates the Examiner's perceived requirement for the DNA molecule of claim 4 to comprise the entire sequence of SEQ ID NO: 1 without intervening sequences. Applicants respectfully submit that the skilled person would be readily apprised of the metes and bounds of claim 4. Nothing more is required under 35 U.S.C. §112, second paragraph. Claim 6 has been amended to recite a nucleic acid encoding a protein having the sequence of SEQ ID NO: 2. The phrase natural allelic variants thereof has been eliminated,

thereby rendering the rejection of claim 6 under 35 U.S.C. §112, first paragraph moot. Accordingly, Applicants respectfully request the withdrawal of the rejection of claims 4 and 6 under 35 U.S.C. §112, second paragraph.

Applicants also submit that the amendment to claim 6 eliminates the grounds for the rejection of this claim set forth at page 9 of the Official Action. It cannot be disputed that Applicants have fully described a nucleic acid encoding SEQ ID NO: 2. Accordingly, the §112, first paragraph rejection of claim 6 should be withdrawn.

CLAIMS 56-58 MEET THE REQUIREMENTS OF 35 U.S.C. §112, FIRST PARAGRAPH

The Examiner has rejected claims 56-58 under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to enable a skilled artisan to make and/or use the invention. Specifically, the Examiner asserts that the specification fails to provide adequate guidance for how to screen a test compound for inhibition of MOAT-mediated transport.

Applicants strenuously disagree with the Examiner's assertion of a lack of enablement. As noted in the MPEP at §2164,

The information contained in the disclosure of an application must be sufficient to inform those **skilled in the relevant art** how to both make and use the claimed invention. Detailed procedures for making and using the invention may not be necessary if the description of the invention itself is sufficient to permit those skilled in the art to make and use the invention.

[Emphasis supplied.]

In § 2164.01, the MPEP continues,

The test of enablement is whether one reasonably

skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.

(Quoting *United States v. Telecommunications, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988).)

Additionally, it is a well settled premise in patent law that a patent need not teach, and preferably omits, what is well known in the art. Lindemann Maschinenfabrik v. American Hoist and Derrick, 221 USPQ 481, 489 (Fed. Cir. 1984).)

The Examiner specifically states that the specification fails to disclose any method for assessing the inhibition of transport afforded by a test compound by measuring restoration of anticancer drug sensitivity or a reduction of transporter mediated cellular efflux of anticancer agents. Applicants respectfully point out that examples of such drug sensitivity assays and anticancer agent efflux assays are described in Zaman et al. (PNAS 91:8822-8826, 1994) which was incorporated by reference into the application. Specifically, the sensitivity of transfected cells overexpressing MRP in the presence of anticancer drugs is shown in Table 1. Additionally, a drug accumulation assay, i.e. an assay capable of determining the ability of a cell to efflux a drug, is described at page 8823, end of column 1. Applicants assert that it would be readily obvious to a skilled artisan to simply perform these assays on cells expressing MOAT-encoding nucleic acids, in the presence and absence of the test compound to determine whether the compound was capable of inhibiting MOAT-mediated transport. Indeed, U.S. Patent No. 5,766,880 at column 29, lines 8 through 62 describes a method similar to the instant invention for testing for compounds capable of inhibiting the activity of MRP by providing cells expressing MRP, incubating with and without the test compound, and testing the sensitivity of the cell to a cytotoxic agent. The aforementioned assays are not)

intended to limit the invention to such embodiments as other assays may be readily employed to ascertain the inhibition properties of the test compound as would be obvious to a skilled artisan.

The Examiner also states that there is "no evidence of record that MOAT-B protein can mediate cellular efflux of any anticancer agent in a cell." Applicants respectfully point out that MRP and cMOAT were, at the time of the invention, characterized as transporters capable of effluxing cytotoxic drugs (see page 57, lines 12 through 22). The high degree of homology seen between MOAT-B and MRP and cMOAT (see Table 1) implicates MOAT-B as a transporter capable of mediating efflux of cytotoxic agents. Applicants also assert that the cytotoxic drug resistance afforded by the expression of MOAT-B could readily be determined by a skilled artisan without undue experimentation by performing the drug sensitivity assays of Zaman et al. as referenced above.

The Examiner also contends that a test compound determined to inhibit MOAT-B gene expression under the control of a promoter other than the natural MOAT-B promoter may not inhibit the activity of the natural MOAT-B promoter in a host cell. Applicants contend, however, that claims 56-58 refer to inhibiting MOAT activity which may or may not involve inhibition of the promoter. Applicants also assert that it would be readily obvious to a skilled artisan to employ proper negative and positive controls in the assays of the invention in which the selected promoter used to express MOAT is linked to a reporter gene for testing on another population of cells. Such a control would allow the skilled artisan to attribute any inhibiting effects associated with the test compound specifically to MOAT (in nucleic acid or proteinaceous form) or to the promoter.

Additionally, the Examiner alleges that the specification fails to provide adequate guidance on how to screen for an inhibitor of MOAT activity *in vivo*. Applicants

respectfully submit that the inhibitor screen as described at page 36, lines 21 through 29 is an *in vitro* assay. Notably, the cells to be screened are referred to as "cell lines" which, by definition, are *in vitro* entity unless injected into a host. Applicants have amended the claims to specifically recite the method as an *in vitro* assay to clarify the invention. Applicants add, however, that while the screen is an *in vitro* assay, compounds identified by the screen may be readily employed by a skilled artisan in an *in vivo* environment (i.e. treating patients) as noted at page 36, lines 23 through 26.

Applicants submit that the disclosure provided in the instant specification is more than sufficient to enable a skilled artisan to practice the invention. For all of the foregoing reasons, Applicants respectfully request the withdrawal of the rejection of claims 56-58 under 35 U.S.C. §112, first paragraph.

CONCLUSION

In view of the amendments presented herewith, and the foregoing remarks, it is respectfully urged that the objections and rejections set forth in the February 13, 2003 Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number given below.

Respectfully submitted,
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By



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